DETAILED ACTION

Prosecution on the merits has been reopened. The species election has been expanded to include Shigella, E. coli, and Mycobacterium.

Claims 14-24, 30-35 and 41-44 have been canceled. Claims 1-13, 25-29, 36-40, 45-48 are pending.

Specification

The title will have to be changed to more closely reflect the claimed subject matter.

Election/Restrictions

This application contains claims, 29 and 40 drawn to an invention nonelected with traverse in the reply filed on 4-23-09. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1-13, 25-28, 36-39 and 45-48 are under consideration as they relate to the species Shigella, E. coli, and Mycobacterium.

Applicant's arguments filed 7-18-11 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-13, 25-28, 36-39 and 45-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for expressing an

immunogen in vivo by administering a Shigella, E. coli, or Mycobacterial host cell to a mammal, wherein said Shigella, E. coli, or Mycobacterial host cell comprises a plasmid encoding an immunogen, wherein the Shigella, E. coli, or Mycobacterial host cell is unable to use its own machinery to express the encoded immunogen, wherein the immunogen is expressed in vivo by cells of the mammal, does not reasonably provide enablement for any polynucleotide encoding an immunogen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1 and 8 encompass expressing a polynucleotide encoding an immunogen in a cell unable to use its own machinery to express the immunogen, wherein the polynucleotide is integrated into the host cell genome. Claims 6, 13 and 45 specifically require the polynucleotide is incorporated into the genome. Such embodiments encompass episomes, viruses, specifically retroviruses, and any other polynucleotide that integrates into the genome. The claims are not limited to plasmids or replicons and are not limited to polynucleotides in the cytoplasm. The specification discusses polynucleotides on pg 4, 2nd paragraph, but the examples are limited to using plasmids. The specification and the art at the time of filing do not support expressing polynucleotides integrated into the genome of a cell in which its own machinery is unable to express the immunogen as encompassed by the claims because other cells' machinery would be required for expression but could not use chromosomal origins of replication found in the inactivated cell or the other cell. Nor could the other cells' machinery even access the nucleus or the polynucleotide integrated into the genome

such that expression occurs. Other cells' machinery simply cannot access the polynucleotide or express the immunogen when the polynucleotide has been integrated into the genome of the cell. Therefore, the claims should be limited to plasmids or replicons or somehow limit the claims to polynucleotides in the cytoplasm.

Claim 48 limits the replicon to an RNA replicon. The specification mentions RNA replicons but does not teach the structure of any such replicons. The specification mentions genomic RNA sequences from viral (e.g. RNA and DNA viruses and retroviruses) (pg 4, 2nd full paragraph. The specification and art at the time of filing does not teach RNA replicons are cytoplasmic, and RNA replicons that integrate into the genome of the cell are not enabled for reasons cited above. Accordingly, the specification fails to provide those of skill with adequate guidance to use RNA replicons to express immunogens as claimed, and it would have required those of skill undue experimentation to determine how to do so.

Response to arguments

Applicants argue the claims as amended overcome the rejection. Applicants' argument is not persuasive because the claims encompass polynucleotide integrated into the host cell genome.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 5, 7-9, 12, 25-28, 36-39, 46-48 are rejected under 35 U.S.C. 102(a) as being anticipated by Li (J. Allergy Clin. Immunol., July 2003, Vol. 112, pg 159-167).

Li taught administering heat killed E. coli comprising a plasmid encoding a peanut antigen to a mouse. The antigen was expressed in the mouse as claimed as evidenced by the immune response. Claim 48 has been included because it limits the replicon but still encompass using a plasmid.

Claims 1, 2, 5, 7-9, 12, 25, 27, 36, 38, 46-48 are rejected under 35 U.S.C. 102(e) as being anticipated by Branstrom (US Patent 5,824,538, US Patent 7,045,336, US Patent 7,235,234) (or 102(b) in the case of '538).

Branstrom taught attenuated Shigella flexneri or any other bacteria including E. coli or mycobacteria for delivery of plasmid DNA encoding an antigen (col. 1, lines 6-17; col. 2, lines 14-22; col. 3, lines 8-16; col. 4, lines 1-10; col. 6, lines 5-15, of '538, for example. The bacteria were heat inactivated (col. 17, lines 34-43; Table 4, in '538, for example). The bacteria do not have to be alive, and the nucleic acids are plasmids can be released into the cells, thereby allowing the cell to express the antigen. The bacteria were administered to a mammal and an immune response was obtained (col. 16, Example 6; col. 18, Table 5; col. 19, Table 6 (see "heat-killed" 15D or 2457T) in '538 for

example). Claim 48 has been included because it limits the replicon but still encompass using a plasmid.

Claim Rejections - 35 USC § 103

The rejection of claims 1, 2, 5-8, 9, 12, 13, 25, 27, 36, 38 and 45-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xu (Vaccine, 2003, Vol. 21, pg 644-648; available online to the public on Oct. 25, 2002 and published Jan. 2003) as supported by zur Megede (J. Virol. 2000, Vol. 74, pg 2628-2635) in view of Masschalck (Applied and Environmental Microbiology, Vol. 67, No. 1, pg 339-344) and Raettig (Zentralblatt fuer Bakteriologie Mikrobiologie und Hygiene 1 Abt originale A, 1981, Vol. 205, No. 4, pg 511-520, abstract only) has been withdrawn in view of applicants' arguments.

The rejection of claims 1-13, 25, 27, 36, 38 and 45-48 under 35 U.S.C. 103(a) as being unpatentable over Xu (Vaccine, 2003, Vol. 21, pg 644-648; available online to the public on Oct. 25, 2002 and published Jan. 2003) as supported by zur Megede (J. Virol. 2000, Vol. 74, pg 2628-2635) in view of Masschalck (Applied and Environmental Microbiology, Vol. 67, No. 1, pg 339-344) and Raettig (Zentralblatt fuer Bakteriologie Mikrobiologie und Hygiene 1 Abt originale A, 1981, Vol. 205, No. 4, pg 511-520, abstract only) as applied to claims 1, 2, 5-8, 9, 12, 13, 23-25, 27, 34-36 and 38 and further in view of Chang (Applied and environmental microbiology, June 1985, Vol. 49, No. 6, pg 1361-1365, abstract only), Kruithof (Proceedings – Annual Conference, American Water Works assoc. 2000, pg 331-344, abstract only) and the applicant-

acknowledged art at the time of filing has been withdrawn in view of applicants' arguments.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-5, 7-12, 25-28, 36-39, 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li (J. Allergy Clin. Immunol., July 2003, Vol. 112, pg 159-167) or Branstrom (US Patent 5,824,538, US Patent 7,045,336, US Patent 7,235,234) in view of Chang (Applied and environmental microbiology, June 1985, Vol. 49, No. 6, pg 1361-1365, abstract only), Kruithof (Proceedings – Annual Conference, American Water Works assoc. 2000, pg 331-344, abstract only), Forney (US Patent 7,001,571) and the applicant-acknowledged art at the time of filing.

Li or Branstrom taught administering inactivated bacteria comprising plasmid DNA encoding an antigen to a mammal (see anticipation rejections above). Li or Branstrom did not teach UV or hydrogen peroxide inactivation.

However, Chang taught inactivating bacteria using UV light exposure (see abstract) and Kruithof inactivated a variety of bacteria using UV light exposure and hydrogen peroxide. Furthermore, applicants acknowledge that inactivating cells was standard in the art at the time of filing including UV light exposure (pg 6, lines 17-19). Forney establishes UV light and hydrogen peroxide were well-known in the art at the time of filing for inactivating bacteria (col. 1, line 49, through col. 2, line 3). These techniques inherently result in bacteria to be "unable to use its own machinery to express the encoded immunogen" as claimed because the cells are inactivated.

Thus, it would have been obvious to those of ordinary skill in the art at the time the invention was made to administer inactivated bacteria comprising plasmid DNA encoding an antigen to a mammal as described by Li or Branstrom using UV light or hydrogen peroxide as described by Chang, Kruithof, Forney, and acknowledged by applicants as being known in the art. Those of ordinary skill would have been motivated to inactivate bacteria using UV light treatment or hydrogen peroxide instead of heat inactivation because Kruithof taught UV treatment and hydrogen peroxide was the "ultimate solution for pesticide control and disinfection" (see title).

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

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